

AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph at page 1, prior to line 4 (which line 4 states "Field of the Invention"):

[0000] This application is a divisional of and claims priority to U.S. Patent Application Serial No. 09/876,185, (now U.S. Patent No. _____) filed June 8, 2001.

Please amend the paragraph beginning at page 2, line 16, as follows:

[0005] Blood filters generally have a blood compartment having input and output ports connected to the blood circuit, a filter membrane, and a filtrate compartment. The membrane separates the blood compartment and the filtrate compartment in the filter. In a filter used primarily for ultrafiltration, the pores of the filter membrane may be hollow fibers having blood passages of approximately 0.2 mm or less in diameter. The filter membrane pass fluids, electrolytes and small and middle sized molecules (typically up to 50,000 Daltons) from the blood plasma. The ultrafiltrate output from the filtration pores is similar to plasma, but without the plasma proteins or blood cells. In an ultrafiltration filter, the concentration of small solutes is the same in the ultrafiltrate as in the plasma, and, thus, no clearance or concentration change is obtained of small solutes in the blood plasma that is returned to the patient. However, the ultrafiltration does remove water from the blood and is useful for treating patients suffering from fluid overload. During the ultrafiltration treatment of a fluid overloaded patient the fluid that is mechanically "filtered" or removed from blood is typically immediately replaced by the access fluid

that has been stored in the body. As a result the excess fluid or “edema” in the legs, the abdomen and the lungs of the patient is reduced and the patient’s condition is relieved.

Please amend the paragraph beginning at page 3, line 24, as follows:

[0008] Generally, all modes of Renal Replacement Therapy involve the removal of blood (typically venous) from a patient and passing the blood through a hollow fiber filter where there occurs fluid removal and, if desired, a solute removal or exchange. After passing through the filter, the blood is returned to the blood stream of the patient. So-called “batch” type RRT devices extract and return blood through the same single lumen IV catheter or “needle” and blood tube by reversing the direction of the blood pump. More common “continuous” type devices extract and return blood continuously using one double lumen catheter in the same vein or separate catheters in two separate veins. Catheter and needles used in RRT are generally known as “blood access”. Some RRT patient patients have permanently lost their kidney function and need to undergo dialysis several times a week. These patients typically have surgically implanted or modified sited for blood access such as arterial-venous shunts or fistulas.

Please amend the paragraph beginning at page 5, line 23, as follows:

[0013] Fluid overload can lead to several painful and dangerous conditions, including excessive fluids in the lungs. If excessive fluid in the lungs is not promptly removed with a diuretic medication, CHF patients are often intubated and placed on a ventilator. If the

initial diuretic therapy has little affect, more aggressive treatment with increasingly potent diuretics is needed. In addition, inotropic agents such as dobutamine are administered to increase the pumping function of the heart and ~~rise~~ raise the blood pressure. Higher blood pressure is expected to assist in the perfusion of the kidneys and make diuretics work. In more recent years, vasodilator therapy became a part of the standard therapy for a severely volume-overloaded, decompensated CHF patient. All the above-mentioned therapies as a rule require admission to an intensive care unit (ICU) of a hospital. Potentially dangerous side affects of drugs and the need for advanced monitoring and intubation are the main reasons for a typical ICU admission. However, ICU admissions are expensive and require specialized doctor and nurse caregivers.

Please amend the paragraph beginning at page 8, line 6, as follows:

[0018] Recently, applicants invented an ultrafiltration technique that relies on peripheral vein access. ~~These~~ This ultrafiltration technique is described in commonly-owned U.S. Patent No. 6,533,747 (~~now pending U.S. Patent Application Serial No. 09/698,132, filed October 30, 2000 (atty. ref. 3659-20)~~) and entitled “Extracorporeal Circuit for Peripheral Vein Fluid Removal”, the entirety of which is incorporated by reference, and in U.S. Patent No. _____ (~~now pending U.S. Patent Application Serial No. 09/618,759, filed July 18, 2000 (atty. ref. 3659-10)~~) and entitled “Method and Apparatus for Peripheral Vein Fluid Removal in Heart Failure”, the entirety of which is incorporated by reference. The volume of blood that can be drawn from a peripheral vein is substantially

less than can be drawn from a central access vein. Nevertheless, the relatively-small volume of blood removed from peripheral veins has been found sufficient for ultrafiltration for most CHF patients suffering from fluid overload.

Please amend the paragraph beginning at page 12, line 28, as follows:

[0031] Theoretically, all veins in the human body are connected. The network of veins in a human body include a trunk vessel (central venous cavity) connected to the right atrium of the heart. From the central venous cavity extend extends many branches of veins that each branch progressively to smaller and smaller veins until the veins become tiny capillaries that connect to the arterial circulatory system. In the venous system, blood drains from the capillaries and flows to the progressively larger veins until all veins drain into the large flow of the central venous cavity. Thus, the largest supply of blood in the venous system is downstream of the blood flow, which is ultimately the central venous cavity. In contrast, the largest supply of blood in the arterial system is upstream because blood flows from the central arteries and downstream towards the capillaries.

Please amend the paragraph beginning at page 15, line 4, as follows:

FIGURE 2 is-a illustrates the placement of the peripheral access venous blood withdrawal catheter in the patient.

Please amend the paragraph beginning at page 16, line 16, as follows:

[0038] In addition, the caliber of peripheral veins 116 in the arm in a person can be 2 to 3 mm. A metal or plastic 16 to 20 Gage phlebotomy needle is commonly used to draw blood for various clinical needs. A standard catheter needle 130 for a peripheral vein phlebotomy can be 25 to 45 mm long. The catheter needle 130 shown in Figure 1 is for blood infusion, but such a needle is also suitable for blood withdrawal from the peripheral vein in a healthy person. However, a catheter needle may not be appropriate for persons having weak peripheral veins. If a 16 Gage needle (approximately 1.65 mm outer diameter) is placed in such a vein it will almost occlude the vein and will be prone to collapse the walls of the vein around it with the application of negative pressure. Also, blood vessels in an arm tend to vasoconstrict (contract) in response to neurological and hormonal stimuli. The patient's motion can intermittently cut off the blood supply.

Please amend the paragraph beginning at page 17, line 13, as follows:

[0040] In view of the limitations described above, fluid removal in volume overloaded CHF patients via a peripheral vein using standard-length phlebotomy needles has been impractical for many CHF patients. Experiments have been conducted for blood withdrawal and infusion using 20 Gage, 18 Gage and 16 Gage plastic needles 35 to 40 mm long inserted in lateral antibrachial, cephalic, basilic and other adjacent surface veins at the arm bend at the elbow of patients. These patients varied widely in body size, age and medical condition. The objective of the experiment was to withdraw blood continuously using a computer controlled roller pump at 40 to 60 mL/min. Blood was

continuously re-infused into a different vein in the opposite arm of the patient. During the experiment, treatment time ranged from 15 minutes to 4 hours. Infusion of 40 to 60 mL/min of blood into almost any vein in the arm or hand of CHF patients was always possible. However, withdrawal of blood from peripheral veins at the same rates of 40 to 60 mL/min was problematic in as many as 50% of CHF patients and impossible in as many as 20% of these patients.

Please amend the paragraph beginning at page 18, line 21, as follows:

[0043] The medical practitioner inserts the catheter using a common medical technique, such as an “over the wire” method or through a hollow introducer needle that is later peeled apart and removed. If access to the right atrium is desired, the length of a typical PICC is 65 cm. If the catheter tip is positioned in a basilic, auxiliary or cephalic vein at the level or just below the shoulder 212, it is often called a “mid-line” catheter and extends approximately 25 cm into the arm venous system.

Please amend the paragraph beginning at page 20, line 7, as follows:

[0048] Moreover, a PICC extends the benefits of mechanical fluid removal by eliminating certain risks that previously limited its use. A PICC catheter 104 is inserted through a peripheral vein 109 in the patient’s arm, in a manner only slightly more complex than the insertion of a common phlebotomy or IV medication needle. When inserted, the tip of the PICC catheter resides in a larger venous vessel 166. Such larger

venous vessels may be just below the shoulder, in the shoulder or in a subclavian vein slightly above the shoulder. Even access to the vena cava or right atrium of the heart are is not out of reach of certain long PICC catheters. Thus, the advantages of the retrograde blood flow, impossible with common catheter needles, become accessible using a PICC catheter.

Please amend the paragraph beginning at page 23, line 16, as follows:

[0056] Modern plastic luer connectors are easy to use, inexpensive and resist sufficiently to the positive pressure inside. Even if small leaks develop in a luer connector under positive pressure owing to poor fit, such leaks usually are not dangerous, easy to identify and can be corrected or tolerated. Luer and Luer lock (ones that can be secured) connectors are not intended to and do not withstand significant negative pressure. When subjected to negative pressures, lure lock connectors frequently leak air bubbles into the blood circuit. Even small amount of air, if infused into a patient, can be dangerous and cannot be tolerated. Since inventors wanted to withdraw blood through a high resistance PICC catheter, standard luer connectors of blood catheters to catheters had to be abandoned in favor of the design that can withstand negative pressure. Similar to traditional ones, the special airtight connectors were made from plastic using inexpensive ejection injection molding technique. Unlike luer connectors, they do not rely on a tight fit of cone shaped male and female parts to establish the seal. Connectors use the silicone rubber gasket as a seal between the coupled parts of the connector. When the connector

is engaged and locked, the seal is compressed. This way the quality of seal is not dependent on the precision of tolerances used in manufacturing of plastic parts.

Please amend the paragraph beginning at page 24, line 5, as follows:

[0057] Connectors using compression gaskets are well known and used in different industrial and commercial applications. Inventors used connectors designed and manufactured by with Colder Products Company (St. Paul, MN). Such connectors were never used previously as a part of a blood access device to connect extracorporeal circuits to catheters for blood treatment. Consequentially there have never been PICC catheters with hubs adapted to connect to such devices. Inventors developed a novel PICC with an airtight connector specifically designed for safe blood withdrawal.

Please amend the paragraph beginning at page 26, line 15, as follows:

[0062] The filter 112 includes a blood compartment 132 134 (Figure 4) having the blood inlet port 124 and the blood outlet port 126. The blood compartment is separated by a filter membrane 134 from a filtrate compartment 136 of the filter. The filter membrane is permeable to water and small molecules. The membrane is impermeable to blood cells, proteins and other large solutes particles. The patient 106, such as a human or other mammal, may be treated while in bed or sitting in a chair and may be conscious or asleep. The PICC withdrawal catheter 104 and return catheter 130 may be attached to

the patient in a hospital, doctor's office or an outpatient clinic (provided that adequate supervision of a doctor or other medically trained person is present).

Please amend the paragraph beginning at page 28, line 5, as follows:

[0066] As shown in FIGURE 1, the ultrafiltration apparatus 100 includes a blood pump console 148 and a blood circuit 102. The console includes a rotating roller blood pump 118 108 and a filtrate pump 150 that move blood and ultrafiltrate fluids through the circuit, respectively, and the circuit is mounted on the console. The blood circuit (detailed in Fig. 4) includes a continuous blood passage between the withdrawal cannula 104 and the return cannula 130. The blood circuit includes a blood filter 112; pressure sensors 152 (in withdrawal tube), 154 (in return tube) and 156 (in filtrate output tube); an ultrafiltrate collection bag 114 and tubing catheters to connect these components and form a continuous blood passage from the withdrawal to the infusion catheters and ultrafiltrate passage from the filter to the ultrafiltrate bag. The blood passage through the circuit is preferably continuous, smooth and free of stagnate blood pools and air/blood interfaces. The circuit may come in a sterile package and is intended that each circuit be used for a single treatment.